# ORIGINAL ARTICLE

# Comparative Evaluation of Intravenous Propofol, Thiopentone Sodium and Ketamine for Short Surgical Procedures.

Veena Asthana, MD,\* Sanjay Agrawal, MD,\* J.P. Sharma, MD\*\*

\*Asst. Professor, \*\* Professor

Department of Anesthesiology, Pain Management & ICU, Himalayan Institute of Medical Sciences, Jolly

Grant, Dehradun (India)

Correspondence: Dr. Veena Asthana, Assistant Professor, Department of Anesthesiology, Pain Management

& ICU, Himalayan Institute of Medical Sciences, Jolly Grant, Dehradun (India)

E mail drvasthana@yahoo.co.in

#### **ABSTRACT**

**Purpose:** The increasing popularity of outpatient surgery has prompted the search for new anaesthetic agent that can provide safe and effective anaesthesia with a rapid and smooth recovery. We compared three induction agents, namely propofol, thiopentone sodium and ketamine to find the most suitable agent for this purpose.

Patients & Methods: This prospective study was conducted at HIMS, Dehradun on 90 ASA I, II patients of either sex and in age group 16-65 years undergoing minor surgical procedures under general anaesthesia not requiring endotracheal intubation. The patients were randomly allocated into three groups of 30 patients to receive either inj propofol 2-2.5 mg/kg IV (Group A), inj thiopentone 3-5 mg/kg IV (Group B), or inj ketamine 1-2 mg/kg IV (Group C).

**Results:** It was noted that the induction time was shortest with Inj thiopentone and recovery was quickest with Propofol. Heart rate, SBP, DBP decreased with injection thiopentone and Propofol being more in case of injection Propofol in comparison to injection to thiopentone. Inj Ketamine led to increase in all the parameters.

Conclusion: Propofol is an ideal choice for short surgical procedures.

Key words: Propofol; Thiopentone Sodium; Ketamine; Induction Agents; Day Case Surgery.

# INTRODUCTION

Today more than 60% of all elective surgeries are performed in the outpatient surgical setting, and it is expected that this number will increase.1This rapid growth in ambulatory surgery would have not been possible without the changing role of the anesthesiologists and the development of more titrable anaesthetic drugs and less invasive surgery.<sup>2</sup>

An ideal outpatient anaesthetic should have a smooth and quick onset of action; produce intra operative amnesia and analgesia, good surgical

conditions with a short recovery period, no side effects leading to early discharge.3 In view of increasing popularity of outpatient surgery search for new anaesthetic agent that can provide safe and effective anaesthesia has been prompted. This study was conducted to compare iv anaesthetic agent Propofol, Thiopentone and Ketamine in short surgical procedures with regard to induction time, effect on vitals, side effects (e.g. nausea and vomiting, hallucination, apnea etc) and recovery profile.

#### **PATIENTS AND METHOD**

This study was conducted at Department of Anesthesiology, Pain Management & ICU, Himalayan Institute of Medical Sciences, Jolly Grant, Dehradun. After obtaining approval from Hospital Ethical Committee and fully informed consent, 90 ASA grade I/II patients of either sexes in the age group of 16-65 years undergoing elective short surgical procedures requiring general anaesthesia without endotracheal intubation were studied. Patients belonging to ASA grade III/IV, morbidly obese haemodynamically unstable and patients with respiratory problem were excluded from the study.

Table I:	Patients	Data	(A ore	Weight	ASA	Grade)	Z.
Table 1.	1 auciits	Data	(Age,	weight,	MOM	Grade)	1

	GROUP A (n=30)	GROUP B (n=30)	GROUP C(n=30)
Male: Female	14:16	17:13	19:11
Age in years Mean±SD Range	34.65 ±8.23 16-55yrs	40.45±7.37 26-55yrs	30.95±5.93 16-4 <sup>/</sup> ਼੍ਰਾਂs
Weight in kg Mean±SD Range	54±6.1 45-67 kg	56±6.8 40-70 kg	49±11 40-80kg
ASA grade I:II	18:12	20:10	19:11
Induction time in seconds Mean±SD	29.2±7.57	25.45±3.7	131.8±36.6

All the patients were kept fasting overnight and were advised tab diazepam 10 mg orally at bedtime and in the morning of surgery with a sip of water. In the operating room after putting iv canula and taking preop vitals, inj glycopyrrolate 0.01mg/kg was given IV. The patients were then randomly divided into three groups of thirty patients each to receive induction either with propofol 2-2.5 mg/kg IV (Group A); with inj thiopentone 3-5mg/kg IV (Group B) or with inj. ketamine 1-2 mg/kg IV (Group C).

In Group A and B loss of eyelash reflex was taken as the end point of induction while in Group C loss of painful reflex was taken as end point of induction. In all the three groups patients were maintained on spontaneous ventilation using Bains circuit with 66% nitrous oxide in oxygen and

incremental dose of the induction agent.

Induction time was calculated as time interval between start of induction and loss of eyelash reflex (Group A, B) and loss of movement to painful stimuli (Group C). Smoothness of induction was judged by apnea, pain, hiccup, myoclonia or any other complication; movements in response to surgery was noted and graded as;

a. None no movement

b. Mild no noticeable by surgeonc. Moderate interrupting the surgeon

d. Severe required abandonment of surgery or

supplementation.

Pulse rate, respiratory rate, systolic and diastolic blood pressure were recorded at preinduction, just after induction, after 2,5 minutes and 10 minutes of induction. Other parameters observed were time of onset of anaesthesia, amnesia, side effects like hallucinations, apnea, PONV and the hospital stay.

The time of recovery from anaesthesia was observed at 15 second intervals after the completion of surgery and any complications during recovery period were noted. Time taken for obeying verbal command on request was noted every 10 minutes after the completion of surgery, by asking the patients to open the eyes, protrude the tongue and to lift the head. The time of sitting on the bed and the time of walking in the straight line was recorded. Each patient

Box 1: Modified post anaesthetic discharge scoring system (MPADSS)<sup>4</sup>

Score Parameter	2	1	0	
Ambulation	steady joint/ no dizziness	with assistance	none/dizziness	
Nausea and Vomiting	minimal	moderate	severe	
Pain	minimal	moderate	severe	
Surgical bleeding	minimal	moderate	severe	

Legend: 2= within 20% of preoperative value; 1 = 20-40% of preoperative value; 0= >40% of preoperative value

was interviewed before leaving the recovery room and questioned about adverse affects like headache, nausea, vomiting, confusion, hiccups etc. The intravenous site was inspected for signs of erythema.

Guidelines for safe discharge from ambulatory surgical facility include stable vitals signs, return to baseline orientation, ambulation without dizziness, and minimal pain, PONV or bleeding at the surgical site. We discharged patients by using the modified post anaesthetic discharge scoring system (MPADSS)<sup>4</sup> which is shown in Box 1.

#### RESULTS

In our study the mean induction time recorded was 29.2±7.57 sec, 25.45±3.7 sec and 131.8±36.6 sec in Group A, B and C respectively (Table I). Mean induction time was shortest in group receiving thiopentone.

There was a decrease in heart rate from preinduction values in Group A at 2 and 5 min, but it returned towards baseline at 10 min. In Group B there was an increase in heart rate than baseline value which remained high throughout the period of observation. In Group C there was an increase in heart rate than

Table II: Heart rate, Mean arterial pressure, respiratory rate (Mean ± SD)

Groups	Pre induction	Onset of induction	2 min	5 min	10 min
Group A	90±6.65	91.1±8.14	88.25±9.28	88.25±9.28	90.60±10.14
Group B	79.60±14.59	88.95±8.93	96.2±9.97	88.21±8.05	84.1±7.8
Group C	93.9±11.53	96.1±11.7	96.4±11.16	98.2±12	98±12
1	MEAN ARTERIA	AL PRESSURE	AT DIFFEREN	NT LEVELS(mm	ıHg)
Group A	96.4±7.40	89.7±6.6	86.4±7.37	83.8±8.24	89.1±6.75
Group B	94.7±7.55	89.1±8.01	87.5±8.09	89.4±7.58	94.5±7.82
Group C	87.6±8.6	92.6±6.4	92.2±6.42	90.4±6.3	87.4±6.9
	RESPIRATORY	RATE AT DIF	FERENT LEVE	LS OF INDUCT	ION
Group A	18.05±2.01	16.5±2.5	14.5±2.5	15.2±2.14	17.4±2.1
Group B	18.4±2.14	17.95±2.48	16.7±2.32	17.25±2.49	18.6±1.73
Group C	16±2.1	14±1.8	14±1.9	14±1	14.1±1.65

pre induction value which remained elevated throughout the period of observation.

There was a significant fall in the mean BP in both Group A and B, but it was more pronounced in propofol group. The initial fall in mean BP returned to preinduction level in Group B. There was a rise in the ketamine group, which was decreased after 10 min.

The mean respiratory rate before induction was  $18.05\pm2.01/\text{min}\ 18.4\pm2.14$ ,  $16\pm2.1$  in Group A, B, C

Table III. Recovery Time (Mean±SD) in Minutes

Groups	Response to verbal commands			Complete recovery		
	Eye Opening	Protrusion of Tongue	Uplifting of Head	Orientation	Sitting	Walking
Group A	4.46±1.1	5.25±1.04	6.9±1.2	7.53±1.3	13.8±3.72	24.1±8.36
Group B	6.6±1.12	8.09±1.27	10±2	13±2.8	18.9±4.99	32.2±9.59
Group C	6.02±.96	7.6±1.5	12.4±1.31	13.85±1.7	23.4±9.01	50.8±24.46

Table IV: Complications during induction and post operative period

Groups	Complications during induction of anaesthesia			Post operative complications		
	Pain at Inj	Excitatory movement	Apnea	Nausea, vomiting	Headache	Confusion
Group A	2	1	2	-	1	-
Group B	1	-	1	2	1	1
Group C	1	-	1	1	1	3

respectively in our study (Table II). There was no significant change in Group A and B, but a slight decrease was noted in Group C, which continued upto 10 minutes without showing any rise towards baseline.

Mean duration of recovery (eye opening) after cessation of anesthetic was at  $4.46\pm1.1$  min in Group A, while in thiopentone group it was  $6.6\pm1.2$  min and in ketamine group  $6.02\pm.96$  min.

Table III shows mean time to eye opening, protrusion of tongue and lifting of head on verbal

command. It also shows signs of complete recovery, e.g. orientation, ability to sit and walk straight.

The incidence of complications noted in three groups on induction and at recovery is given in Table IV.

#### **DISCUSSION:**

Ambulatory surgery has become increasingly popular during the past two decades due to an increased demand in cost saving, fewer beds occupancy, its popularity with the patients due to minimal separation from family and less disruption in personal life, and a rapid return to daily activities. There is reduced risk of wound infection, deep vein thrombosis, pulmonary embolism and pneumonia.

The ideal anesthetic agent for ambulatory surgery should have a smooth and rapid induction, fast recovery, intraoperative amnesia and analgesia and minimal side effects post operatively.7 Thiopentone is traditionally associated with rapid induction, short duration of action and minimal side effects. However, poor psychomotor recovery and subjective feeling of tiredness and drowsiness associated with it in the post operative period limits its usefulness in day case patients.8 Ketamine is a good anesthetic agent as it has a rapid onset of action, intense analgesia and intact laryngeal reflexes, making it the agent of choice even in full stomach patients. The disadvantages, however, are cardio stimulatory effect, emergence delirium and hallucinations postoperatively.9 It also has been associated with increased pulmonary resistance. These complications can be somewhat minimized if a benzodiazepine is used prior to Ketamine anaesthesia. 10 Propofol is highly lipid soluble and produces rapid onset of anesthesia with quick recovery due to its short elimination half life and high lipid clearance rate.11 This makes it particularly suitable for use in outpatient anaesthesia.

In our study the mean induction time recorded was 29.2±7.57 sec, 25.45±3.7 sec and 131.8±36.6 sec

in Group A,xB,C respectively (Table I). This is consistent with the study of Richard Johnson et al<sup>12</sup> who found the induction was faster with thiopentone in comparison to propofol.

Hemodynamic variable such as heart rate (Table II) showed that in propofol group there was an increase in heart rate immediately post induction followed by decrease in heart rate at 2min and 5 min with return towards baseline 10 min. Thiopentone and Ketamine group heart rate was increased throughout the period of observation. These findings are consistent with the findings of many earlier studies. <sup>13-16</sup>

Mean arterial blood pressure (Table II) showed that there was a significant fall in blood pressure from preinduction value in both propofol and thiopentone group while there was a rise in Ketamine group. These findings are consistent with findings of Grounds et al<sup>17</sup>. The fall in blood pressure in thiopentone Group A and Group B than ketamine group. This fall in BP is due to fall in systemic vascular resistance while increase seen in ketamine group is due to sympathomimetic effect of ketamine itself. Monedero Rodriguez P et al<sup>18</sup> observed that propofol 2mg/kg caused a significant fall in arterial blood pressure (greater than thiopentone in DBP) and a decrease in heart rate (thiopentone did not change heart rate).

The mean respiratory rate before induction was 18.05±2.01/min 18.4±2.14, 16±2.1 in Group A, B, C respectively in our study. In Group A, there was a fall seen in the values at 2 min and 5 min but at 10 min RR returned to the baseline while in Group C fall in the value continued up to 10 minutes.(Table II); whereas various investigators reported that propofol was more respiratory depressant than thiopentone in equipotent doses.<sup>19-21</sup>

Immediate recovery criteria used such as eye opening on command, tongue protrusion and head lifting was found to be faster in propofol group than

in thiopentone and ketamine group. Delayed recovery observed in PACU was also faster with proposol and patient was able to sit without support, fully oriented at 7.53±1.3 min and 13.8±3.72 min respectively (Table III).

It has been recommended that propofol induction resulted in a faster awakening of patients and better recovery function compared with thiopentone for the first 240 minutes after the procedure.<sup>22</sup> Time taken by patient to sit without vertigo and walk in a straight line was less in patients receiving propofol and patient was shifted from recovery at a much quicker time than with other groups. However in other groups the recovery was delayed being worse in Ketamine group.

It was recommended that post anaesthesia recovery was superior with propofol, with virtual absence of side effects and rapid recovery, with little impairment of psychomotor function 30 minutes after anaesthesia. None of the patients reported any awareness during anaesthesia and all found course of anaesthesia acceptable in the three groups.

Richard Johnson et al<sup>12</sup> also reported faster recovery with propofol as compared to thiopentone group. They observed remarkable clear headedness of the patients recovered from propofol. Redistribution is the principal mechanism for early awakening after a single dose of induction agents used. According to Kalman et al there was no difference in the results of early or late recovery tests but patients receiving propofol experienced fewer post operative symptoms and were more cheerful. Propofol compared to thiopentone and Ketamine was associated with a short time discharge from the recovery room.

Complications such as pain on injection, apnea, excitatory movement were more significant in propofol group than in other groups (Table IV). Pan was found at the site of injection in two propofol group but it was not severe and did not require

discontinuation of anaesthesia. Only one patient in thiopentone and Ketamine group suffered pain. Mc Collum et al<sup>25</sup> compared four intravenous agents, thiopentone, propofol, etomidate, methohexitone and found least pain at the site of injection with thiopentone.

Mild excitatory movements were noted in one patient in propofol group these movements did not interfere with induction. None of the patients induced with thiopentone and ketamine showed involuntary movements. Similar to our study Mc Collum<sup>25</sup> noted mild, transient excitatory movements with propofol as compared to methohexitone, etomidate and thiopentone. In ketamine the induction was smooth with no excitatory phenomenon as reported in previous studies <sup>26</sup>.

Apnea more than 20 sec was noted in 2(6.67%) in propofol and 1(3.33%) in both ketamine and thiopentone group. Mc Collum and Dundee reported higher frequency of apnea following induction with propofol as compared to thiopentone. <sup>25-29</sup> Incidence of nausea and vomiting were more in thiopentone group as compared to Group A and C. White, Ding and Borgeat et al noted the incidence of nausea and vomiting to be low 3% and similar in both thiopentone and ketamine. <sup>28-30</sup>

As far as post anaesthetic level of consciousness was concerned, propofol proved to be best. Almost all patients fulfilled the criteria for adequate recovery. Overall assessment highlighted the efficacy of propofol, with its better recovery profile; while there was not much to choose between thiopentone and propofol. According to Borgeat A, the interval between the end of administration of propofol or thiopentone and extubation, as well as discharge to the ward was significantly shorter with propofol. <sup>30,31</sup>

### **CONCLUSION:**

Thus in conclusion propofol has a rapid and smooth induction, short duration of action and

quick, pleasant and clear headed recovery with minimum side effects, better street fitness and least hospital stay time. Propofol due to its quick recovery profile is a better replacement for thiopentone and Ketamine in short surgical procedures.

## REFERENCES:

- 1. White PF. Use of Ketamine for sedation and analgesia during injection of local anaesthesia. Annals of Plastic Surgery 1985; 15:53-6.
- 2. Lee TW. PBn during injection of Propofol. The effect of prior administration of thiopentone. Anaesthesia 1994; 49:817-818.
- 3. Bassil A, Jabbour A, Khourys, Baraka A. Propofol versus thiopentone for induction of anaesthesia in patient undergoing outpatient surgery. Middle East Journal of Anaesthesiology 1989;(10):307-14.
- 4. Chung F. Are discharge criteria changing? J. Clin Anaesth 1993; 5: 645.
- 5. Ohtersen HB Jr, Clatworthy HW Jr. Outpatient herniorraphy for infants. Am J Dis Child 1968; 116:78
- 6. Gregory GA. Outpatient anaesthesia. Anaesthesia Ist edition. Edited by Miller RD. New York, Churchill Livingstone.1981:1323-1333.
- 7. Dawson B, Reed WA. Anaesthesia for adult surgical outpatients. Can Anaesth Soc J 1980; 27:409.
- 8. Berggren L, Eriksson I. Midazolam for induction of anaesthesia in outpatients-A Comparison with Thiopentone. Acta Anaesthesiol Scand 1981; 25:492.
- 9. Carrel R. Ketamine A general anaesthetic for unmanageable ambulatory surgery. J. Dent Child 1979;40: 288.

- 10. Perel A, Davidson JT. Recurrent hallucinations following Ketamine. Anaesthesia 1976; 31:1081.
- 11. Johnson R, Noseworthy T. Propofol versus Thiopentone for outpatient. Anaesthesiology 1987; 67:431-435.
- 12. Grounds RM, Maxwell DL, Taylor MB, Aber V, Royston D. Acute ventilatory changes during IV induction of anaesthesia with thiopentone and Propofol in man. BJA. 1987; 59: 1098-1102.
- 13. Doze VA, White PF: Effects of fluid therapy on serum glucose levels in fasted outpatients. Anaesthesiology 1987;66:223,.
- 14. Moore J, Cll KM, Flynn RJ, McKealing KJ, Howard PJ. A comparison between Propofol and thiopentone as induction agents in obstetric anaesthesia. Anaesthesia 1989; 44:753-757.
- 15. White PF, Vasconez LO, Mathes SA, Way WL, Wender LA. Comparison of midazolam and diazepam for sedation during plastic surgery. Plastic and reconstructive surgery. 1988; 81:703-12.
- 16. Grounds RM, Twigley AJ. The haemodynamic effects of intravenous induction: Comparison of the effects of thiopentone and Propofol. Anaesthesia. 1985; 40:735-740.
- 17. Mondero RP, Panadero SA, Garcia PF, Carrera HJ Catal JC, Arroya CJL. Comparative study between thiopentone and Propofol in short duration anaesthesia. Anaesthesia Reanim 1991; 38:153-5.
- 18. Goodman NW, Black AMS, Carter JA. Some ventilatory effects of Propofol as sole anaesthetic agent .BJA, 1987; 59: 1497-1503.
- 19. Taylor MB, Ground RM, Mulrooney PD, Morgan M. Ventilatory effect of Propofol during induction of anaesthesia.:A comparison with thiopentone Anaesthesia .1986; 41: 816-820.

- 20. Mc Collum JSC. The antiemetic action of Propofol.Anaesthesia:1988; 43:239-240.
- 21. Health PJ, Ogg TW, Gilks WR .Recovery after day case anaesthesia. A 24 hour comparison of recovery after thiopentone or Propofol anaesthesia 1990;45:911-5.
- 221. Macenzie N, Grant IS: Comparison of the new emulsion formulation of Propofol with methohexitone and thiopentone for induction of anaesthesia in day cases. Br J Anaesth1985; 57:725.
- 23. Kalman CJ, Drummond JC: Monitors of depth of anaesthesia, Quo Vadis? Anaesthesiology 2002;96: 784.
- 24. Cartwright PD, Pingal SM. Midazolam and diazepam in Ketamine a anaesthesia. 1984; 39: 439-42.
- 25. Dundee JW, Ghaly RG, Cll KM: Effects of

- stimulation of P6 antiemetic point on postoperative nausea and vomiting
- 26. White PF: Are non pharmacological techniques useful alternatives to antiemetic drugs for the prevention of nausea and vomiting? Anaesth Analg 84: 712, 1997.
- 27. Ding Y, Fredman B, White PF: Use of mivacurium during laparoscopic Surgery: effect of reversal drugs on postoperative pBn recovery. Anesth Analg 1994; 78:450,.
- 28. Borgeat A, Fuchs T, Tassonyi E: Induction characteristic of 2% Propofol in children.BJA 1990; 78(4) 433-5.
- 29. Borgeat A, Popovic V,Meir D, Schewander D:Comparison of Propofol and thiopentone /halothane for short duration ENT surgical procedures in children. Anaesth Analg 1990; 71:511-5.

